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Quantification of cigarette tar exposure and lung cancer risk: Aspects of prevention and early detection

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Lung cancer epidemiology has undoubtedly led to some of the most important results in cancer research. Among many other findings the clear dose-response relationship between tobacco consumption and lung cancer risk offers interesting areas not only for further research but also for intervention techniques. Acknowledging the fact that lung cancer treatment has already established its possibilities and no dramatic progress is to be expected, we have to focus our interest on prevention and early detection of this man made cancer.

The modern lung cancer epidemiology provides not only ideas on how to improve lung cancer control but also first answers to important questions in this field. Some examples are as follows: (a) Prevention of lung cancer is possible in the order of 85% of all cases, complete abstinence from tobacco consumption in a given population being the theoretical background. (b) Ever increasing evidence shows that lung cancer risk could also be lowered by either changing individual smoking habits and/or by modification of the tobacco product, especially the cigarette. While these possibilities cannot be compared with the benefits of non-smoking, they have to be taken into consideration too because millions of people still smoke and millions of youngsters will start in the future. (c) The epidemiology of lung cancer in the decades to come will definitely show whether the concept of reducing the cancer risk among smokers is working in terms of noticeable changes in morbidity. (d) Screening for lung cancer – if it is to be of any benefit – has to be designed according to the epidemiological findings. High-risk groups are to be screened, such groups being defined according to the smoking histories of the individuals involved.

Our contribution will hopefully be of some help in both areas: prevention and early detection; it is an analysis of lung cancer risk in relation to the life long tar exposure in cigarette smokers. Our considerations are also based on the numerous retrospective and prospective epidemiological studies already available including our own work. In a nationwide retrospective study, lung cancer patients and appropriate controls were interviewed about all relevant life style factors (6, 7). This work led us to the development of a formula for quantifying tar exposure (10) which will be demonstrated further on.

In the course of the epidemiological investigations on lung cancer in

Austria, we detected two important circumstances: (a) The average smoking history of the smokers and smoking lung cancer patients is not homogenous as far as daily consumption and favourite brands are concerned. The considerable changes in smoking habits among the relevant age groups should be observed and taken into account. Due to economic reasons and other factors,. e.g. availability of cigarettes during and after the WWII, daily consumptions are not relatively stable variables for epidemiologists. (b) The cigarette market underwent important changes during the last decades; especially, the tar content of cigarettes decreased considerably. This has to be considered as well, along with the switching of brands with different tar contents during the life-long smoking career of a tobacco consumer.

These considerations are derived mainly from the local Austrian situation which is undoubtedly different from the tobacco market and the smoking habits in e.g. the U.S.A. where many studies have been conducted in the past.

CALCULATION OF TAR EXPOSURE

The current and previous cigarette brands were grouped into three categories according to their tar yields (Group I: below 15 mg, Group II: 15-24 mg, Group III: more than 25 mg). The tar yields used are those determined and published by the Austrian Tobacco Monopoly (1). The problem of the relatively high tar yield figures obtained by the measurement procedure used in Austria is solved by implementing factors for each group (Group I = 1, Group II = 2, Group III = 3). The formula itself uses information about all brands ever smoked, their specific tar yield, the duration of, and all variations in daily consumption (10).

$$TE = \sum_{ij=1}^{n} (a_{x_i} b_{x_j}) k_x + \sum_{ij=1}^{n} (a_{y_i} b_{y_i}) k_y + \sum_{ij=1}^{n} (a_{z_i} b_{z_i}) k_z$$

where a_x, a_y, a_z = cigarette consumption per day in Groups I-III; b_x, b_y, b_z = years of cigarette consumption in Groups I-III; and k_x, k_y, k_z = group factor.

Thus, for example, a smoker who smoked 30 high-tar cigarettes/day (Group III) for 20 years, 2 packs/day of another brand of Group III for 14 years. 2 packs/day of a medium-tar cigarette (Group II) for 9 years, and 1 pack/day of a low-tar cigarette (Group I) for 1 year has a tar exposure of 4220. The calculation is: 30 (cigarettes) x 3 (group factor) x 20 (years) = 1800 + 1680 (40 x 3 x 14) + 720 (40 x 2 x 9) + 20 (20 x 1 x 1).

This formula is a first step and, of course, only additional information and is not meant to replace the usual analysis by the known variables. It is also incomplete and could be supplemented by information about inhalation, butt length and other characteristics of tobacco apart from tar yields.

In contrast to many remaining problems with this formula, some unsolveable questions and the possible and given disadvantages of any simplification

of a very complex situation, some favorable aspects of a simple quantification of tar exposure should be mentioned: (a) rather complex and changing smoking habits may be described more easily than by other means; (b) the changing market structure and the changing tar contents of cigarettes can be implemented into statistical analysis; (c) high-risk groups may be identified more easily and accurately, and thus the resources can be better aimed at those groups which are extremely exposed smokers; (d) for health education purposes a simple formula might be quite impressive for tobacco consumers and would add motivational elements to the precessation process; (e) last but not least, the formula might be helpful in trying to define a threshold for lung cancer risk in smokers. The discussion about this topic is now in progress and remains one of the most important scientific problems in the area of applied cancer research.

TAR EXPOSURE: RESULTS AND EXAMPLES OF APPLICATION

The following should demonstrate how quantitative information about the tar exposure to smokers could be used to: compare lung cancer patients and controls; show differences between male and female patients and controls; calculate relative risks of smokers compared to non-smokers; contribute to the question of possible thresholds of lung cancer risk; check how actual smoking habits are related to these thresholds; identify high-risk groups for screening.

Lung cancer patients and controls

The average tar exposure in male tumor patients is significantly higher than the tar exposure in controls. Using the smoking histories of 414 patients and 828 controls in all age groups (395 or 95% of the cases being smokers or ex-smokers compared to 620 or 75% of the controls) the following average tar exposures were calculated: 2596 for smoking cancer patients, 2026 for smoking controls (significant at $P < 1\%$). There is also a significant difference between Kreyberg I tumors (TE 2616), squamous cell carcinoma cases (TE 2628) and controls, but not between Kreyberg II tumors (TE 2421) and controls.

In the age groups 51-60 and 41-50 respectively, we found the same distribution pattern of tar exposure, although the absolute figures are somewhat different due to the relatively shorter smoking careers especially in the youngest age group.

Female patients and controls

The average tar exposure in a female tumor patient is significantly higher than the average tar exposure in female controls; but it is significantly lower than the average tar exposure in a male patient.

Using the smoking histories of 200 patients and 400 controls (117 or 59%

of the cases being smokers or ex-smokers compared to 86 or 22% of the controls) the following average tar exposures were calculated: 1824 for smoking cancer patients, 1200 for smoking controls (significant at $P < 1\%$). There is also a significant difference between Kreyberg I tumors (TE 1874), squamous cell carcinoma cases (TE 1662) and controls, but not between Kreyberg II tumors (TE 1579) and controls.

In Austria lung cancer in females is less frequent than in males because the percentage of tobacco consumers is lower in females than in males, and moreover, the average tar exposure in the female smoker is lower than that in the male smoker. Both factors contribute to the fact that less females compared to males are at high-risk for lung cancer.

The years to come will show a continuous rise in lung cancer morbidity among females since the smoking habit is still spreading (in contrast to males) and the average daily consumption is increasing (11).

Relative lung cancer risk for smokers

Tar exposure is of course related to lung cancer risk in a dose-response relationship – Table 1 gives the figures for males and females (9, 10, 12). Most interesting is the fact that tar exposure and risk for Kreyberg II tumors are also linked in females.

Question of thresholds

It has already been stated clearly that non-smoking is the optimal strategy to prevent lung cancer. Discussing thresholds of lung cancer risk should never lead to the conclusion that continuation of smoking is a good advise to tobacco consumers under certain circumstances. But reality presents the picture of the smoking epidemic and therefore we have to discuss what we can achieve for those who cannot or do not want to stop smoking.

We strongly believe in a comprehensive and complex system of intervention to control lung cancer which, among other strategies, also includes product modification of cigarettes (3, 8). Lowering tar yields is one of the most important goals in this respect.

Checking our results in order to contribute to the question of thresholds of lung cancer risk, one identifies tar exposures in the range of 500-1000 which might be of help in discussing the point further. This tar exposure range has to be compared with the actual situation of smoking habits in order to find out whether it is a realistic and feasible goal.

If the average Austrian smoker smokes the leading brand for 30 years with a daily consumption of 30 cigarettes he gains a tar exposure of 1800. This is still quite a high exposure. A young smoker who starts with a low tar cigarette and smokes only one pack per day and stops after 20 years gets a tar exposure of 400 which is in the range of a possible threshold for lung cancer risk. This assumption of a smoker's career is quite realistic because low tar brands are relatively popular among young smokers. But there are still the hard-core smokers, especially among the less educated males, who

Table 1 Lung cancer risk and tar exposure (9, 10, 12)

Tumor types	Tar exposures < 500	501-1000	1001-2000	2001-3000	3001-4000	4001-5000	> 5001
Males: All age groups							
All cancer types	1.6	2.4^{+}	4.2^{+}	5.8^{+}	6.1^{+}	7.4^{+}	6.1^{+}
Kreyberg I	2.0	2.6^{+}	5.3^{+}	7.2^{+}	7.7^{+}	9.5^{+}	7.8^{+}
Kreyberg II	—	1.8	1.8	3.5^{++}	> 3001:3.9		
Age 41-50 yr							
Kreyberg I	0.6	2.4	6.3^{+}	9.1^{+}	4.6^{++}	4.6^{++}	6.1^{++}
Kreyberg II			> 1001 : 2.1				
Age 51-60 yr							
All cancer types	0.8	2.1	6.5^{+}	9.0^{+}	8.7^{+}	6.6^{+}	8.4^{+}
Kreyberg I	1.0	4.1^{++}	15.7^{+}	21.5^{+}	20.8^{+}	17.1^{+}	21.5^{+}
Kreyberg II	0.6	1.0	1.2	3.3	3.0	—	—
Females: All age groups					> 3001		
All cancer types	1.1	2.1^{+}	3.5^{+}	3.3^{+}	3.2^{+}		
Kreyberg I	1.5	4.2^{+}	4.8^{+}	4.9^{+}	6.8^{+}		
Kreyberg II	—	1.1	3.1^{+}	—	2.3^{++}		

$^{+}P < 1\%$; $^{++}P < 5\%$.

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prefer non-filter, high tar cigarettes and who have been smoking at least a pack per day for an average of 35 years. Such smoking history gives a tar exposure of over 2000 and makes the individuals concerned candidates for lung cancer.

Identification of high-risk groups for screening

Early detection of lung cancer is related to the chance of cure, and the organization of screening programs is now a topic of intensive scientific and public discussion. Recently, the American Cancer Society released rather pessimistic statements about the value of screening for lung cancer.

Based on the epidemiological situation in Austria and first experiences of the Mayo-Lung-Project (2), we calculated that in a high-risk group of smokers (more than 20 cigarettes a day for more than 20 years) 1.4% lung cancer cases could be detected by an intensive screening program including X-ray and cytology. Undoubtedly, the application of our formula for tar exposure could lead us to a more precise definition of people at extreme risk. These should be screened first, also because of the excess morbidity caused by other tobacco related diseases.

It is not lung cancer alone which supports the need for special health check-ups for heavy smokers. Therefore, we developed PROGRAM 20 x 20 (20 cigarettes daily for 20 years) which focuses on several tobacco related diseases including lung cancer and also offers a smoking withdrawal treatment to the client (4, 5).

SUMMARY

A formula to quantify the tar exposure in smokers is described; it is based on information about the life-long smoking habits of the individual and offers some aspects to the prevention and early detection of lung cancer: rather complex and changing smoking habits may be described more easily than by other means; the changing market structure and the changing tar content of cigarettes can be implemented into statistical analysis; high-risk groups may be identified more easily and accurately, and thus the resources can be better aimed at those groups which are extremely exposed smokers; for health education purposes a simple formula might be quite impressive for tobacco consumers and would add motivational elements to the precessation process; last but not least, the formula might be helpful in trying to define a threshold for lung cancer risk in smokers. The average tar exposure in male tumor patients is significantly higher than that in controls. There is a significant difference between Kreyberg I tumors, squamous cell carcinoma cases and controls but not between Kreyberg II tumors and controls.

The average tar exposure of a female tumor patient is significantly higher than the average tar exposure of female controls; but it is significantly lower than the average tar exposure of a male patient. Tar exposure is of course related to lung cancer risk in a dose-response relationship.

To contribute to the question of thresholds of lung cancer risk, one identifies tar exposure which might be of help in discussing this matter further.

The application of the formula for tar exposure could lead to a more precise definition of people at extreme risk. These should be screened first, also because of the excess morbidity caused by other tobacco related diseases.

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